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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,111	09/17/2003	Patrick Bernardelli	PC25382A	9341

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PFIZER INC.
PATENT DEPARTMENT, MS8260-1611
EASTERN POINT ROAD
GROTON, CT 06340

EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 07/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,111	BERNARDELLI ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,5,6,8-11 and 13-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,5,6,8-11 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5-11-06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

Applicant's amendment of 5-11-06 has been fully considered.

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5-11-06 has been entered.

Claims 1, 2, 4, 7 and 12 have cancelled.

Claim 18 has been added.

Claims 3, 5, 6, 8-11 and 13-18 are pending.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 3, 5, 6, 8-10 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

a. Claim 18 recites variable R and its definition (in the definition of R^2). However, R is not in any of the substituents listed for $(C_1\text{-}C_6)$alkyl group. Thus, it is unclear what relationship R has with formula (I).

b. Claims 3, 5, 6, 8-10 and 13-17 are rejected as being dependent on claim 18 and carrying over the unrelated variable R.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement** (for hydrates and solvates): Claims 3, 5, 6, 8-11 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making "*hydrates*" and "*solvates*" of the claimed compounds. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims: Claim 18 recites "hydrates" and "solvates" of compounds represented by formula (I). The terms "hydrates" and "solvates" covers various forms of the same compound at different proportions of water or solvents. Thus, the scope of claim 18 is unduly broad.

Claims 3, 5, 6, 8-11 and 13-17 depend on claim 18 for the scope of formula (I), and thus also have the broad scope of "hydrates" and "solvates" as well.

The amount of direction or guidance presented: The specification does not define or describe proportions of water for hydrates, and does not list what solvents are suitable for solvates. There is no working example for making a hydrate or solvate. Thus, the specification fails to provide sufficient enablement for making "hydrates" and "solvates" of the claimed compounds.

1. **The state of the prior art:** Although it is not unusual to expect a "hydrate" or "solvate" of a compound, the process for selecting a hydrate or solvate is not standard for all drugs. For the claimed compound, there is no reference teaching any possible hydrate or solvate. Thus, the state of the prior art does not support the broad scope of "hydrates" and "solvates" in claims 3, 5, 6, 8-11 and 13-18.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in extensive research to select a particular "hydrate" or "solvate"

for each compound from the large Markush group of formula (I). Not only one has to determine an IC_{50} value, but also *in-vivo* activity to establish an LD_{50}, therapeutic index for each hydrate or solvate as well as physical properties (e.g., solubility). Given a large Markush group of formula (I), such a task would require a tremendous amount of effort, time and resource.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The process of making a "hydrate" and "solvate" is quite unpredictable because it is not possible to predict whether solid solutions will form and at what stoichiometry proportion (i.e, one, two, or half a molecule of solvent added per molecule of host).

Thus, with such a limited teaching from the specification and the art, the skilled chemist would have to engage in undue experimentation to make the hundreds of thousands of compounds covered by "hydrates" and "solvates" of compounds represented by formula (I) in claims 3, 5, 6, 8-11 and 13-18.

3. **Scope of Enablement:** Claims 13-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of AIDS does not reasonably provide enablement for the treatment of other diseases such as: *T-cell related diseases, osteoporosis, COPD, asthma, cancer, leukemia, allergy, dermatoses, psoriasis and atopic dermatitis.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The breadth of the claims:

Claim 13 recites specific diseases such as: *T-cell related diseases, autoimmune diseases,*

osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, acquired immune deficiency syndrome (AIDS), allergy, dermatoses, psoriasis, atopic dermatitis.

Claim 14 depends on claim 13, but only recites *asthma, allergy or atopic dermatitis.*

Claim 15 depends on claim 13, but only recites *osteoporosis.*

Claim 16 depends on claim 13, but only recites *cancer.*

Thus, together, the scope of claims 13-16 covers the treatments of many diseases that affect different organs or systems such as: bones, joints, immune system, lungs, skin, neurological system, colon, stomach, pancreas, etc. All of the cited diseases have different underlying factors. The treatment of one might even be contraindicated in the other.

The amount of direction or guidance presented: The specification only provides a reference for the *in-vitro* assay of the inhibition of PDE7. Compounds #1-6 were disclosed to have IC_{50} of less than 1 μM, which is much too general for an IC_{50}. The specification does not show evidences for the treatments of the following diseases:

i. No evidence shown for an effect on T-cell to treat T-cell mediated diseases.

ii. No evidence shown for brochiodiation, or mast cell inhibition for the treatment of COPD, asthma or allergy.

iii. No evidence shown for an increased bone density to treat osteoporosis.

iv. No evidence shown for the inhibition of mitosis to treat cancer.

v. No evidence shown for an increased production of erythrocytes to treat leukemia.

vi. No correlation shown between PDE7 inhibition and the treatment of dermatoses, psoriasis, etc.

In short, the specification does not provide sufficient guidance for the skilled clinician to use the claimed compounds in the treatment of many diseases that are allegedly related to the inhibition of PDE7.

The state of the prior art: As evidence by the reference of Bricher et. al. (EP 530,994 A1), the spiro-quinazolinone compounds are disclosed as a possible permutation that can inhibit HIV reverse transcriptase. Thus, following such a teaching, at best, the skilled clinician could only use the claimed compounds in the treatment of AIDS.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the use of the claimed compounds in the treatment of *T-cell related diseases, autoimmune diseases, osteoporosis, chronic obstructive pulmonary disease (COPD), asthma, cancer, leukemia, acquired immune deficiency syndrome (AIDS), allergy, dermatoses, psoriasis, atopic dermatitis*. Because each of those diseases have different underlying factors and manifestation, to find an effective dose for each compound to treat all those diseases would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only discloses that the claimed compounds have IC_{50} of less than 1 μM. However, said evidence does not adequately guide the skilled clinician in the treatment of diseases that would require the treatment of other underlying factors that are not

related to PDE7. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claims 13-16.

Double Patenting

The **nonstatutory double patenting** rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 3, 5, 6, 8-11 and 13-18 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 29-34, 36-45 and 47 (or final claims 1-6, 8-17 and 19) of the recently allowed U.S. Application No. 10/ 852,404 . Although the conflicting claims are not identical, they are not patentably distinct from each other because instant formula I overlaps with formula I of the allowed application having the following substituents:

i. X_1, X_2, X_3 and X_4 is CR^1;

ii. R^1 is Q_1;

iii. Q_1 is hydrogen, halogen or OR^2;

iv. X is NR^9; R^9 is hydrogen;

v. Y is NR^{12}; R^{12} is hydrogen;

vi. Z is O;

vii. A is a 5-, 6- or 7-membered ring.

Note, some species in claim 44 of the allowed application anticipate the instant formula I with substituents corresponding to those cited above.

The instant formula I differs from formula I of the allowed application by not having other alternatives for R^1 (e.g., X^5R^5), or other alternatives in place of Z (e.g., S or NR^{13}), or A as an 8-membered ring. However, such a difference constitutes a difference in scope only. Thus, it would have been within the level of one skilled in the art to recognize that the instant formula I is a subgenus of formula I of the allowed application. Therefore, it would have been obvious to select the claimed compound in view of formula I of the allowed application.

No pending claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M, T and Th (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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7-20-05

Tamthom N. Truong
Examiner
Art Unit 1624

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600